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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/530,871 | 04/11/2005 | Hans-Georg Kreysch | MERCK-2990 | 4478 |

23599 7590 02/21/2007

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| EXAMINER | |
|---|---|
| HUYNH, PHUONG N | |
| **ART UNIT** | **PAPER NUMBER** |
| 1644 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 31 DAYS | 02/21/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/530,871 | KREYSCH ET AL. | |
| | Examiner | Art Unit | |
| | Phuong Huynh | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *One* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 April 2005*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-29* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

I. The following is noted.

For restriction purpose, the "use" claim 29 is prosecuted as "methods of use".

II. Claims 1-29 are pending.

### *Election/Restrictions*

III. Restriction to one of the following inventions is required under 35 U.S.C. 121 and 372:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1:

1. Claims 1-28, drawn to **a pharmaceutical composition** comprising a first and a second antibody molecule, or a portion thereof, having the capability to bind to different epitopes located on the same or different ErbB receptor molecule types, wherein said first antibody molecule or a portion thereof, comprises binding sites that bind to a first specific epitope on the ErbB 1 receptor molecule type, and said second antibody molecule comprises binding sites that bind to a second specific epitope on the same ErbB 1 receptor molecule type, a kit comprising said first and second antibody molecules.

2. Claim 29, drawn to **a method of using a pharmaceutical composition** or a pharmaceutical kit comprising a first and a second antibody molecule, or a portion thereof, having the capability to bind to different epitopes located on **same** ErbB receptor molecule types, wherein said first antibody molecule or a portion thereof, comprises binding sites that bind to a first specific epitope on the ErbB 1 receptor molecule type, and said second antibody molecule comprises binding sites that bind to a second specific epitope on the same ErbB 1 receptor molecule type for manufacture of a medicament to treat tumors or tumor related diseases.

The inventions listed as Groups 1-2 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The WO 94/00136 publication (of record, January 1994; PTO 1449) teaches a composition comprising a combination of a first and second anti-erbB-2 such as monoclonal, chimeric, bispecific and/or single chain antibodies or binding fragment thereof that bind to different epitopes located on the same ErbB2 receptor (see claims 1-3 of the WO 94/00136 publication, page 6, DETAILED DESCRIPTION OF THE INVENTION, page 8, lines 1-24, in particular). The reference antibodies bind to the extracellular domain of the natural ligand binding domain (see page 12, lines 6-7, in particular) and inhibit tyrosine phosphorylation signaling (see page 10, second full paragraph, in particular). The WO 94/00136 publication teaches that a combination of anti-receptor antibodies leads to different and more potent anti-tumor activities than single antibody (see page 10, last paragraph, in particular).

The invention in claim 1 differs from the teachings of the reference only in that the pharmaceutical composition wherein the first and second antibodies bind to different epitopes located on the same ErbB1 receptor instead of ErbB2 receptor.

The US Pat No 5,705,157 (issued Jan 6, 1998; PTO 892) teaches various monoclonal antibodies specific for the extracellular domains of EGFR (ErbB1) such as Mab 425 and antibody to ErbB2 such as 7.16.4 for treating tumor (see entire document, col. 4, lines 64-67 bridging col. 5, lines 1-7, Abstract, in particular). The '157 patent teaches a combination of antibodies work synergistically to suppress tumor growth (see col. 3, lines 10-15, in particular).

The US Pat 4,943,533 (issued July 1990; PTO 8792) teaches various monoclonal antibodies such as Mab455 and Mab 225 that bind to the different epitope on the same epidermal growth factor receptor (ErbB1) where one antibody competes with the ligand for binding to the receptor and the other antibody binds to the receptor but does not compete with the ligand (see entire document, col. 3, line 46-53, col. 8 through 10, in particular). The reference antibody 225 inhibits the growth of A-431 tumor cells in the absence of ligand (see col. 8, lines 15, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art with the expectation of success in substituting the anti-erbB-2 antibodies in the pharmaceutical composition for treating tumor as taught by the WO 94/00136 publication for the Mab 425 antibody that binds to ErbB1 as taught by the '157 patent and the Mab 225 antibody that binds to

ErbB1 as taught by the '533 patent for use as a medicament for treating tumor. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the WO 94/00136 publication teaches a combination of anti-receptor antibodies can lead to different and more potent anti-tumor activities than single antibodies (see page 10, last paragraph, in particular). The '157 patent teaches that Mab 425 antibody that binds to ErbB1 is useful for treating tumor and a combination of antibodies work synergistically to suppress tumor growth (see entire document, col. 4, lines 64-67 bridging col. 5, lines 1-7, Abstract, see col. 3, lines 10-15, in particular). The '533 patent teaches that monoclonal antibody 225 that binds to EGRF1 (ErbB1) inhibits the growth of A-431 tumor cells in the absence of ligand (see col. 8, lines 15, in particular).

Since Applicant's inventions do not contribute a special technical feature when viewed over the prior art they do not have single general inventive concept and lack unity of invention.

IV. Accordingly, Groups 1-2 are not so linked as to form a single general inventive concept and restriction is proper.

V. Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

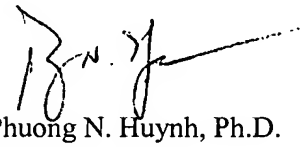
VI. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until all claims to the elected product claim are found allowable, an otherwise

proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

VII. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

VIII. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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February 20, 2007